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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/034,015	LOUGHNEY, KATE	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants preliminary amendment of the specification, cancellation of claims 3-33 and the addition of new claim 34, Paper No. 5, 12/20/2001, is acknowledged. Claims 1, 2 and 34 are at issue and are present for examination.

Priority

Applicants amendment of the first line of the specification to state that this application is a divisional application of U.S. patent application Serial No: 09/256,000, filed February 23, 1999 which claims priority of U.S. Provisional Application No. 60/075,508, filed February 23, 1998, is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Specification

The disclosure is objected to because of the following informalities:

Applicants amendment of the first page of the specification which recites "... application of U.S. patent application Serial No: 09/256,000, filed February 23, 1999 which claims priority of U.S. Provisional Application No. 60/075,508, filed February 23,

1998..." It is suggested that applicants amend this capitalizing "**P**atent **A**pplication" so as to maintain consistency.

The summary of the invention recites "preferred polypeptides comprise the amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:18, SEQ ID NO:20 and SEQ ID NO:22"(page 4, line 2 - line 42). SEQ ID NOs 18, 20 and 22 are all nucleic acid sequence not amino acid sequence.

Appropriate correction is required.

Claim Objections

Claims 1, 2 and 34 are objected to because of the following informalities:

Claims 1 and 34 each recite "PDE10 polypeptide". It is suggested that the first time in the claims this is recited that if be written out in full followed by the abbreviation in parenthesis such as phosphodiesterase 10 (PDE10).

Claim 2 is drawn to a polynucleotide according to claim 1 or 2. Claim 2 is drawn to a polypeptide of claim 1 comprising the amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:18, SEQ ID NO:20 and SEQ ID NO:22. SEQ ID NOs 18, 20 and 22 are all nucleic acid sequence not amino acid sequence.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 34 is rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter. In the absence of the hand of man, naturally occurring polypeptides are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "An isolated and purified human PDE10 polypeptide ..." .

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (claim 2 dependent on) is indefinite in the recitation of "PDE10" as the specification fails to teach which identifying characteristics distinguish a "PDE10 polypeptide" from other phophodiesterase proteins. The application teaches that the PDE10 family is distinguished from previously known PDE families in that it shows a lower degree of sequence homology than would be expected for previously identified PDE families and fails to define which characteristics are necessary for inclusion of a protein which is distinct in sequence from Seq ID No: 2 to be considered to be within this class.

Claim 34 is indefinite in the recitation of "moderately stringent hybridization conditions" as the specification does not define what conditions constitute "moderately stringent". While page 8, line 17-20 of the specification describes some conditions which are intended to be moderately stringent, there is nothing to suggest that other conditions would not also be included within the scope of this term and in the art what is considered stringent varies widely depending on the individual situation as well as the person making the determination. As such it is unclear how homologous to the sequence of the reference polynucleotide, a sequence must be to be included within the scope of this claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 34 are directed to all possible PDE polypeptides (claim 1) and all possible human PDE10 polypeptides encoded by a polynucleotide which hybridizes to the non-coding strand of the polynucleotide which encodes amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 20 and SEQ ID NO: 22 (See above claim objections) (claim 34).

The specification, however, only provides four overlapping polynucleotide molecules isolated from a human fetal brain cDNA library and the encoded proteins as representative species encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these polypeptides by any identifying structural characteristics or properties other than sequence, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claim, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1 and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a protein having phosphodiesterase activity and having the amino acid sequence of SEQ ID NO: 2 , does not reasonably provide enablement for any PDE 10 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1 and 34 are so broad as to encompass any possible PDE10 polypeptide (claim 1) and any possible human PDE10 polypeptide encoded by a polynucleotide which hybridizes to the non-coding strand of the polynucleotide which encodes amino acid sequences of SEQ ID NO: 2, SEQ ID NO: 18, SEQ ID NO: 20 and SEQ ID NO: 22 (See above claim objections and rejections under 112 second paragraph) (claim 34). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims, including all PDE10 polypeptides and variants thereof as well as any PDE10 polypeptide encoded by a polynucleotide which hybridizes to the polynucleotides encoding the polypeptides of claim 2 under the specified "moderately stringent hybridization conditions". Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly

intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure a protein having phosphodiesterase activity and having the amino acid sequence of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any PDE10 polypeptide because the specification does not establish: (A) regions of the protein structure which may be modified without effecting phosphodiesterase activity; (B) the general tolerance of phosphodiesterases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a phosphodiesterase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain phosphodiesterase activity and the fact that the relationship between the sequence of a

peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any PDE10 polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Fisher et al. (U.S. Patent No: 5,922,595).

Fisher et al. teach the isolation, cloning as well as nucleic and amino acid sequence of a new cyclic GMP phosphodiesterase. While Fisher et al. call the new phosphodiesterase, phosphodiesterase 9A (PDE9A), the examiner believes that PDE9A is the same molecule or at the very least is a member of the same family as PDE10 of the instant application based on the extremely large amount of identity shared between the molecules disclosed in the instant application and those taught by Fisher et al. Fisher et al. teach a 1997 nucleotide cDNA molecule (SEQ ID NO: 2) that encodes a 593 amino acid polypeptide (SEQ ID NO: 1). The instant application discloses a 1548 nucleotide cDNA molecule (SEQ ID NO: 1) that encodes a 466 amino acid protein (SEQ ID NO: 2). Additionally, longer, overlapping cDNAs (SEQ ID NOs: 18, 20 and 22) are also disclosed by the instant application. A comparison of Fisher et al.'s SEQ ID NO: 1 and SEQ ID NO:2 of the instant application reveals that amino acid sequence between amino acid 21 and 466 of the instant application is identical except for a single mismatch. The protein taught by Fisher et al. extends an additional 148 amino acids in the NH_3-terminal direction. The nucleic acid sequence that encodes these additional NH_3-terminal amino acids shares a large amount of identity with the nucleic acid sequence of SEQ ID NOs: 18, 20 and 22. In addition to the disclosed nucleic and amino acid sequences, Fisher et al. also teach fragments of those SEQ ID NOs, the majority of which would hybridize with those polynucleotides disclosed by the instant application, as well as expression vectors, host cells transformed with said nucleic acids and methods of producing the polypeptide encoded by said nucleic acids.

Therefore, claims 1 and 34 are anticipated by Fisher et al.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
May 16, 2003